

EDITORIAL**NATURE'S HISTORIC GAP: THE 20th CENTURY OF LYMPHOLOGY**

As lifelong “lymphomaniacs,” we were pleased to see the recent News Feature in *Nature* (1) on “unlocking the drains,” i.e., penetrating the lymphatic system’s mysteries. In recounting the latest exciting molecular discoveries flowing from the Human Genome project and related transgenic technology, the author summed up the history of modern lymphology as a “flurry of interest around 1900” and nothing much “until about ten years ago.” In fact, this historical gap – the 20th century – encompassed landmark progress on: mechanisms of lymph formation (microcirculatory fluid and macromolecular fluxes); lymphocyte trafficking and protein recirculation through the lymphatic system (blood-lymph loop); ultrastructural basis of lymphatic absorption; intrinsic lymphatic contractility and pacemaker activity; lymphatic system phylogeny and ontogeny; lymphatic endothelial cultures; in vivo human lymphatic visualization with vital dye, oil contrast, and radionuclide lymphangiograms; regional lymphatic anatomy and physiology (lung, heart, intestine, liver, etc.); lymphatic circulatory and compositional alterations in experimental and human conditions ranging from cirrhotic ascites, heart failure, and fat malabsorption, to renal transplantation,

rheumatoid arthritis, hemorrhagic shock, AIDS-Kaposi sarcoma, and congenital and acquired lymphedema-angiodysplasia syndromes; lymphatic transport of microorganisms; and sustained efforts to assess and control lymphogenous cancer spread (and defense) beginning with radical lymphadenectomy/lymphectomy and gradually more conservative approaches using sentinel lymph nodes as markers of disseminated cancer. In 1966, in response to this mid-20th century explosion of knowledge, the International Society of Lymphology (ISL), now representing 42 nations, was founded to dispel the notion that the lymphatic system was just “lymph nodes held together by strings” and to provide a forum for interested basic scientists and clinicians. At approximately the same time, in rapid succession, three epic tomes appeared covering this new discipline (2-4). The ISL journal *Lymphology* is now in its 38th volume, and 20 biennial International Congresses of Lymphology with Proceedings and many satellite meetings have been held on every continent but Antarctica, attended by tens of thousands, and watched by an enlarging percentage of the hundreds of millions worldwide with lymphatic disorders, particularly tropical

filariasis. As lymphatic vascular biology and lymphangiogenesis research evolved during the 1980's and 1990's, these conferences featured investigations by “molecular lymphologists” (including some Nature mentioned) alongside clinical lymphologists developing non-invasive multimodal lymphatic imaging, diagnostics, and surgical and non-surgical therapeutic approaches to lymphedema and other lymphatic disorders. Now, with the daunting task of translating basic lymphology from “mice to men” and genes to cures, today’s molecular breakthroughs need to be placed in the context of 20th century progress in lymphatic system biology. Indeed, as knowledge accumulates, we recognize how much we don’t know and how far we must travel together to unlock the vexing mysteries of the lymphatic system and its disorders. Finally, over the centuries since Aselli’s discovery of the “chyliferous vessels,” study of the lymphatic system has been challenging, frustrating, confrontational, and even maddening, but never, as suggested in the *Nature* article, “boring” until recently. In the words of “evo-devo” (evolution/development) expert of his day, OF Kampmeier, summing up his life immersed in “lymph” (the divine clear fluid captured by nymphs to fill the vessels of the gods but never mortals), “The lymph vessels, so unimpressive when they were first pointed out to me in 1909 under the microscope — but, I was soon to discover, so elusive or baffling to everyone who had studied them — have lost none of their tantalizing nature in all these years.”

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